REMARKS

I. Amendment

Reconsideration of rejections in the Application is respectfully requested. Upon entry of the foregoing amendment, claims 1, 2, 5, 7-12 and 44-53 will remain pending. Claim 1 has been amended without prejudice in order to expedite prosecution. Therein the word "comprising" has been changed to "consisting essentially of". In addition, the parenthetical clause "(a polyacrylamide which includes) has been deleted based on this change. Applicants respectfully request entry of the above amendment and submit that the amendment does not introduce new matter.

Basis for this amendment is found on page 9, line 2, wherein it describes the hydrogel itself being prepared by the combining process and the relevance of the molar ratio of the physical properties of the hydrogel itself "The hydrogel having the desired physical properties has been obtained by combining acrylamide and methylene bis-acrylamide in a ratio of…".

Turning to the Office Action Claims 1, 2, 5, 7-12 and 44-53 stand rejected. The bases of rejection are addressed in the section below.

II. Claim Rejections

The rejections made against the claimed invention and the traversal thereof is as follows.

35 U.S.C. 103(a) Rejection of Claims 1-2, 5, 7-12, 44-46 and 48-53 based on Annis

The Examiner has rejected Claims 1-2, 5, 7-13, 45 and 48-53 of the invention based on Annis et al (EP 0 248 544 A1). According to the Examiner, it allegedly would have been obvious to one having ordinary skill in the art to "have [produced a bio-stable hydrogel having the]properties claimed" (elasticity and viscosity etc),. The Examiner further concludes that the invention is unpatentable based on her statement that it allegedly is not inventive to discover the optimum or workable ranges by routine experimentation. The Examiner cites In re Aller 220.F.2d 454,456, 105 USPQ 233,235 (CCPA 1955) in alleged support of the rejection.

The Applicant respectfully disagrees and submit for the reasons below that the prior art does not provide the requisite incentive to arrive at stable hydrogels having the claimed properties.

In particular Annis does not teach or suggest the invention as set forth in any one of independent Claims 1, 51 and 52 or the claims dependent thereon. In fact Annis actually teaches away from the claimed biostable hydrogels and therefore the invention could not have been achieved by routine optimization of Annis as suggested by the Examiner.

Firstly, Annis explicitly teaches that the water content of the hydrogel as defined by the claims of the present invention would not be appropriate for a prosthetic device and furthermore Annis also teaches that the viscosity of the hydrogel as defined by the claimed invention would not be appropriate for a prosthetic device.

With respect to the water content of their disclosed hydrogels Annis explicitly states that "The choice of the specified composition for the body has been made to provide, as far as possible, those *properties considered to be appropriate for the related prosthetic role*" (page 2, left column, lines 16-19). Annis continues (lines 43-52) "In development of the invention to date, various cross-linked synthetic polymer hydrogels have been made which can provide most of the desired properties, but the specific water content has proved to be effectively critical in respect of pressure transmission and encapsulation. Water content of a lesser order is associated with a stiffness which adversely attenuates pressure transmitting capability. In fact the specified water content is preferably about 95%". He immediately thereafter warns of having excessive water (page 3, left column, lines 1-5) "However, this development also shows that a body of homogeneous composition at the specified water content has an *inadequate* tear resistance for purposes of securement by sutures during surgery."

Therefore, based on the above teachings, construed in light of the Annis patent as a whole, it is clear that by warning as to the disadvantages of a high water content, that Annis clearly would suggest to a skilled artisan that a low solid weight content would not be favored and in fact is not appropriate for such a prosthetic device. Therefore, the invention is not the result of routine experimentation and optimization as the claimed water content is contraindicated from the reference teachings.

By contrast, and not suggested by Annis, the claims of the present invention define a solid weight content of 0.5 to less than 3.5%. This is contrary to the teaching of Annis which taught that low solid weight contents would not be "appropriate for the related prosthetic role".

Moreover, there would be no incentive for a skilled artisan to modify the teachings of Annis and arrive at biostable hydrogels as claimed. This is because the disadvantages of a low

solid weight content taught by Annis are not issues relevant for the present invention. The hydrogel defined by the claims of the present invention have a complex viscosity of 10 to 700 Pas. As understood by the person of ordinary skill in the art, hydrogels with said complex viscosity are fluid solids. Accordingly, control of water content/solid weight content as a means of determining the physical parameter "tear resistance" is not relevant to the present invention, which deals with a fluid substance.

Accordingly, Annis teaches against lowering the solid weight content to the range defined in the present claims in order to make a suitable prosthesis since such as low solid weight content would not, according to Annis, provide an appropriate physical parameter (tear resistance), said parameter not relevant in the defined viscosity of the claimed invention.

Therefore, based on at least the foregoing Applicant therefore respectfully disagrees with the Examiner's position that the present invention is the result of mere optimization of the workable ranges taught by Annis. Rather, this conclusion is erroneous as it ignores the fact that the claimed invention possesses properties, i.e., water content and viscosity which are not inherent to the Annis compositions and moreover are contraindicated by the teachings of Annis as the claims require a lowering the solid weight content and providing a type of prosthesis not contemplated or suggested by Annis.

In addition, the material or physical properties of the Annis compositions versus the present invention biostable hydrogels support a conclusion that the claims are patentable over Annis. Particularly, Annis teaches that "The choice of the specified composition for the body has been made to provide, as far as possible, those *properties considered to be appropriate for the related prosthetic role*" (page 2, left column, lines 16-19). Further to teaching the disadvantages of too high a water content (see teachings quoted supra), he continues (page 3, left column, lines 5-7) "This deficiency is resolved ... by the provision of localized reinforcements at appropriate edge portions of the body..." Annis explains (lines 39-42) that " In order to enhance the tear resistance of the body 11 for the purposes of securement by sutures, pledgets 12 of polypropylene mesh reinforcement are embedded into the longitudinal end portions...". Annis teaches the use of a solid polyacrylamide body, which requires further rigidification and reinforcement by use of pledgets and sutures, to avoid tearing due to the low tear resistance of solid body.

However, there is no teaching or direction in Annis that rendering the prosthesis fluid, as defined by the claimed viscosity, would provide "*properties considered to be appropriate for the related prosthetic role*". Rather, Annis teaches the contrary, i.e., that it is desirable to find means to render the solid body more rigid. By contrast, the present invention goes against the teaching of Annis by providing a more fluid device thereby providing a type of prosthesis not contemplated or suggested by Annis. The Applicant therefore respectfully disagrees with the Examiner's position that the present invention is a mere optimization of workable ranges taught by Annis.

The claimed invention is further not suggested by Annis based on differences in the cross-linking of the claimed biostable hydrogels which are not suggested by the reference. With respect thereto, Claim 1 defines that "the acrylamide and methylene bis-acrylamide are combined in a molar ratio of 150:1 to 1000:1" [underlined for emphasis].

Annis, instead on column 3, lines 34-38, describes the solid polymer material as being prepared by employing "typically 0.1% by weight, of methylene-bisacrylamide" Assuming that this percentage is in relation to the acrylamide content, which is believed to be reasonable, this translates to a molar ratio of over 10.000:1 of acrylamide to methylene bis-acrylamide. Accordingly, Annis teaches the use of much less cross-linking agent than is contained in the endoprosthetic hydrogel product provided by the claims of the present invention.

Based on this assumption it further reasonably follows that it is logical to presume that the Annis product would be much less cross-linked than the hydrogel of the present invention. Intuitively, one of ordinary skill would presume that the less cross-linked product of Annis would be less solid [than the inventive endoprosthetic hydrogel compositions]. Yet, surprisingly, the opposite is true, i.e., the present invention relates to a fluid material whereas the teachings of Annis instead are limited to a rigid solid.

Therefore, based on the teachings of Annis, it would not be obvious to one of ordinary skill in the art that a hydrogel having the claimed viscosity would be suitable for use as a prosthetic device and furthermore it would not be obvious that a hydrogel possessing such relatively low viscosity would itself be suitable as a prosthetic device and/or that it could be obtained by combining acrylamide to methylene bis-acrylamide in a molar ratio of 150:1 to 1000:1 as claimed herein.

Therefore, based at least on these enumerated differences the obviousness rejection of Claims 1-2, 5, 7-12, 44-46, and 48-53 based on Annis is unsustainable and should be vacated.

35 U.S.C. 103(a) of Claims 1-2, 5, 7-12, 44-46, and 48-53 based on Purkait

The Examiner has further rejected claims 1-2, 5, 7-12, 44-46, and 48-53 of the invention as allegedly being obvious over the teachings of Purkait (EP 0 895 785 A2). According to the Examiner, it would have been obvious to one having ordinary skill in the art to "have [produced biostable hydrogels having the] properties claimed" (elasticity and viscosity etc). Also, the Examiner again, erroneously, concludes that the invention is not inventive on the basis that it purportedly relates to the discovery of the optimum or workable ranges which could be achieved by routine experimentation. The Applicant respectfully disagrees as such conclusions are not supported by the teachings of the reference.

The Applicant respectfully submits that independent claim 1 and the claims dependent thereon are not obvious based on the teachings of Purkait based on any or all of the following. Firstly, Purkait teaches a hydrogel material which based on their teachings must be encapsulated rather than describing a material which may serve itself as an endoprosthesis. Secondly, Purkait teaches against the use a bio-stable hydrogel and instead teaches the use of a material which can be eliminated. Thirdly, the hydrogel material taught by Purkait has 3 components, wherein the minority component may be a cross-linked polyacrylamide whereas claim 1 [as amended herein] instead is directed to a hydrogel which consists essentially of a cross-linked polymer. Instead, in the cross-linked polymer of Purkait this material is used in combination with linear polymer component whereas in the present invention the hydrogel consists essentially of a cross-linked polymer. Fourthly, in the Purkait reference, the teaching of a combined use of a cross-linked material with a low cross-linking density, combined with linear polymer hydrogel would not motivate a skilled artisan to use a more highly cross-linked polymer hydrogel as in the claimed invention. For at least the foregoing reasons the invention as set forth in independent Claim 1 and the claims dependent thereon is not rendered obvious over the teachings of Purkait.

For similar reasoning, the Applicant submits that independent claims 51 and 52 are not obvious over the teachings of Purkait. For one thing Purkait teaches a hydrogel material which must be encapsulated rather than a material which may serve itself as an endoprosthesis.

Secondly, Purkait again teaches against the use a bio-stable hydrogel and instead teaches the use of a material which can be eliminated. Thirdly, the Purkait teaching relating to the combined use of a cross-linked material with a low cross-linking density, combined with linear polymer hydrogel would not lead one of ordinary skill in the art to use a more highly cross-linked polymer hydrogel. These differences are described in further detail below.

1. Filling Material – Physical Properties

The substantial differences in the invention endoprosthetic composition versus the materials described or suggested in Purkait are evident upon obtaining an understanding of the physical properties and the filler material which are decried therein. Particularly, Purkait describes the use of polyacrylamide in a filling material which is contained in an implantable prosthesis wherein such filling material is housed in a shell or membrane (page 3, lines 26-38). By contrast, the claims of the present invention relate to a hydrogel having very different physical properties which is intended and which is itself suitable for use as a prosthetic device.

The viscosity and other parameters recited in inventive claim 1 allow for the gel to be used as an injectable endoprosthesis (see claim 44), as well as used in a shell. Moreover, the hydrogel of the present invention is itself suitable for use as a prosthetic device.

Based on this critical and noteworthy distinction, the properties required by the hydrogel of the present invention cannot be derived from or "optimized" from the teaching of Purkait since these gels serve very different purposes. Whereas the physical properties of the gel of the present invention must provide a material which in itself is suitable as a prosthetic device, providing material which mimics the tissue in terms of texture and resilience (viscosity and elasticity); by contrast, in the device taught by Purkait such device instead derives much of its appropriateness for usage as a prosthesis from the shell texture, e.g., by using conventional shells.

It would be well understood by a skilled artisan that the providing of a hydrogel for use as an endoprosthesis has different requirements, at least in terms of viscosity and elasticity, than a filling material which is to be used, for instance, in a silicone shell. Therefore, the hydrogel defined by the claims of the present invention cannot be seen as an optimization of the teaching of Purkait since it would require changes not suggested based on the disclosed purpose of the Purkait materials as a filler material, not for direct usage as an endoprosthetic material as in the

present invention.. There is no teaching in Purkait which would provide any incentive to produce a biostable hydrogel as claimed possessing appropriate physical properties that would render the hydrogel itself, i.e., without the need for encapsulation, to be suitable for use as an endoprosthesis as claimed herein..

2. Biocompatibility

The claimed biostable hydrogel further differs from Purkait in terms of differences relating to biocompatibility based on their different usages. As noted, Purkait teaches the use of a biocompatible hydrogel as a filling material. Particularly, Purkait teaches the use of a material, as a filling material for a shell, which must have acceptable elimination properties (see page 3, line 8). The material taught by Purkait must be compatible with the shell since leakage and bleeding is to be avoided (see page 3, lines 26-38). Otherwise stated, contact of the material with the tissue is to be avoided.

By contrast, the present invention claims instead are directed to a material which is itself used as an endoprosthesis. Furthermore, the filler material taught by Purkait does not inherently function as an endoprosthesis material. In particular, even assuming that it unintentionally leaks from the shell and comes into contacted with tissue, given the anticipated negative consequences of this undesired event this is minimized since the material (see page 2, line 57- page 3, line 2) "is either excreted from the body, or is easily metabolized into harmless byproducts. Non-metabolized materials must be sufficiently small that they can be transported through membranes and excreted by the body in the urine or fecal matter".

Therefore, whereas the material by Purkait is biocompatible in that it can be metabolized and excreted quickly; instead in the present invention the claims are directed to a hydrogel material which is "bio-stable". In other words, the material defined by the claims of the present invention provides for a stable hydrogel (i.e., when utilized over prolonged usage as an endoprosthesis)... This is contrary to the teaching of Purkait which seeks to avoid contact of the material with tissue and, failing to do so, the material must be suitable for elimination. Accordingly, there is no teaching in Purkait which would incentivize a skilled artisan to make a bio-stable material as claimed, rather the contrary is taught. Indeed, the person of ordinary skill in the art is led away from the teaching of the present invention by the teaching of Purkait.

The validity of Applicants' arguments is furthermore supported by the reference teachings exemplified on page 8 lines, paragraphs [0058] and [0060] where they purport to teach

the "advantageous" rapid elimination of 98% and 95%, respectively, of the polyacrylamide filling material.. Therefore, it is quite clear that Purkait teaches against the permanent prosthesis of the presently claimed invention in that it teaches against the use of a bio-stable hydrogel which is itself used as an endoprosthesis and which therefore must be stable for prolonged duration when used as such.

3. Three Component Filling Material

The claimed invention further differs from Purkait in the nature of the disclosed filler material. As noted previously, the filer material taught by Purkait has 3 components: a first is a water-soluble polymer or hydrogel which may be linear or cross-linked polymer; a second is also water-soluble polymer that has a molecular weight below the renal threshold; and the third component is saline. By contrast, the biostable hydrogel of the present invention as defined by claim 1 as amended herein consists essentially of a polymer of acrylamide which has been cross-linked and water or an aqueous solution. The present invention does not comprise the second component required by Purkait. Specifically, the hydrogel of the present invention is not a mixture of polymer hydrogels. Accordingly, Purkait does not explicitly or inherently teach or suggest a cross-linked polymer of acrylamide which is suitable, by itself, i.e., without combination with a linear polymer, for usage as a prosthetic device.

In addition, in Purkait one of the two polymers contained in Purkait's filling material is described as comprising 1 to 9% of the total weight of the gel. For example, the filling material in Example A comprises 2 grams of cross-linked polyacrylamide and 8 grams of linear polyacrylamide, thus comprising 10% by weight of the total weight of the filling material. Only 2% of the material is cross-linked polyacrylamide. Purkait therefore discloses the need to combine linear polyacrylamide with cross-linked polyacrylamide, with 80% of the polymer being linear polyacrylamide, in order to prepare a material suitable as a filling material in an endoprosthesis. Accordingly, Purkait does not teach that a cross-linked polymer of acrylamide is suitable, by itself, i.e., without combination with a linear polymer, is appropriate for usage as a prosthetic device.

The invention is further not suggested by Example B which describes only the use of linear polyacrylamide. Rather, the hydrogel of the present invention consists of crosslinked polymer, not a linear hydrogel and not a mixture of hydrogels, the cross-linked polymer of the invention itself having the desired physical properties, i.e., without the need for combining with

linear material and without the need for encapsulation in a shell as in the Purkait invention. Accordingly, for at least the foregoing reasoning, there is no teaching in Purkait that cross-linked polymerized hydrogel of acrylamide and methylene-bis-acrylamide is suitable, without combination with linear polymers, to provide a hydrogel possessing the suitable physical properties for its usage as a prosthetic device. Accordingly, the person of ordinary skill in the art is not led to prepare a hydrogel consisting essentially of cross-linked acrylamide as claimed in the present invention.

4. Cross-linked Material

Yet additionally the Purkait reference does not suggest a crosslinked material as claimed herein. Moreover, the 20% component of the filler which may be a cross-linked polyacrylamide in Purkait does not teach or suggest the biostable hydrogel of the present invention. With respect thereto, it should be noted that the first component hydrogel of Example A describes a cross-linked polyacrylamide (which makes 20% of the solid weight of the hydrogel) comprising 0.04% cross-linker (it is ambiguous from the reference whether this is in terms of moles or weight). By contrast, the claims of the present invention define a biostable hydrogel having a molar ratio of acrylamide to methylene-bis-acrylamide ranging from 150:1 to 1000:1. This translates to about 0.1 % to 0.67%, in terms of moles.

Accordingly, the person of ordinary skill in the art would understand from the patent reference that the first component is not to be highly cross-liked, relative the hydrogel of the present invention. Furthermore, the person of ordinary skill in the art would understand from the Purkait patent reference teachings that the cross-linked polyacrylamide component in Purkait is more fluid than the cross-linked hydrogel of the present invention. Consequently, notwithstanding the relatively high fluidity of the first component, the person skilled in the art would be taught that in order to make an even more fluid hydrogel would be achieved by combining the cross-linked polyacrylamide with a low cross-linking density with an even more fluid linear polyacrylamide. Accordingly, the person of ordinary skill in the art is not led to the molar ratio of acrylamide to methylene-bis-acrylamide of 150:1 to 1000:1 to prepare a hydrogel for use as a prosthetic device and in fact is taught way from the use of such a ratio.

Therefore, the rejection based on Purkait should be vacated based on any one or all of the following reasons discussed in detail above i) Purkait teaches the need for a shell in order to

obtain desired physical properties rather than a hydrogel itself being used a prosthetic device; ii) Purkait teaches against the use of a bio-stable hydrogel as defined in the present claims; iii) Purkait teaches the use of a filling material using 80% linear polyacrylamide and 20% cross-linked polyacrylamide rather than the use of a hydrogel of cross-linked polymer of acrylamide itself; iv) Purkait describes a cross-linked polyacrylamide with less cross-linker than the present invention, and combines it with a more fluid linear polymer, the present invention goes against the teaching of Purkait by providing a type of prosthesis not contemplated by Purkait. Moreover, it is further apparent based on the foregoing that the present invention is not a mere optimization of workable ranges taught by Purkait. But rather relates to a biostable hydrogel possessing very different properties than the compositions disclosed or suggested by Purkait.

35 U.S.C. 103(a) Rejection of Claim 47 Based on Purkait (Id.) in view of Vogel

The Examiner has further rejected claim 47 as allegedly being obvious over the teachings of Purkait in view of Vogel. (US Patent No. 6,660,301). Dependent claim 47 of the present invention further limits independent claim 1 by providing for the inclusion of cells for engraftment. For at least the reasons discussed supra, Purkait teaches against the present invention. There is no teaching in view of Vogel, in discussing the use of cells, that renders claim 47 obvious alone or in conjunction with Purkait as this reference does not cure any of the afore-discussed deficiencies of the Purkait reference.

Based thereon the rejection of Claim 47 based on Purkait in view of Vogel should be withdrawn.

CONCLUSION

For at least the reasons stated above, claims 1, 2, 5, 7-12 and 44-53 are in condition for allowance. Accordingly, Applicants respectfully request that the Application be allowed and passed to issue.

In the event any outstanding issues remain, Applicants would appreciate the courtesy of a telephone call to Applicants' undersigned representative to resolve such issues in an expeditious manner.

It is believed that no additional fees are due in connection with this Response. However, in the event it is determined by the U.S. Patent and Trademark Office that additional fees are due, the Commissioner is hereby authorized to charge such fees to the undersigned's Deposit Account No. 50-0206.

Respectfully submitted,

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